IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Antonius Arnoldus Christiaan Jacobs, et al.
Serial No:	10/731,724
Filed:	December 8, 2003
For:	Use of Bacterium for Manufacture of a Vaccine
Confirmation No:	5481
Group Art Unit:	1633
Examiner:	Dr. Sumesh Kaushal
Attorney Ref:	1999.452 US C1

November 6, 2009

APPEAL BRIEF

Mail Stop: Appeal
Board of Patent Appeals
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir/Madam:

Pursuant to Appellants' July 8, 2009 Notice of Appeal, Appellants appeal the claim rejections from the February 9, 2009 Final Office Action. In support of this appeal, Appellants provide the following information, argument, and fee in accordance with 37 C.F.R. §41.37 and MPEP §§1205 and 1205.02.

A request to extend the date to file the Appeal Brief by two months, to November 8, 2009, and authorization for payment was submitted with a Supplemental Response on November 5, 2009.

TABLE OF CONTENTS

I. REAL PARTY IN INTEREST (37 C.F.R. §41.37(c)(1)(i))

The real party in interest in this appeal is Intervet International B.V. This ownership is evidenced by assignment documents recorded at Reel 014791, Frame 0334 (recorded on December 8, 2003); and Reel 018490, Frame 0365 (recorded on November 8, 2006).

II. RELATED APPEALS AND INTERFERENCES (37 C.F.R. §41.37(c)(1)(ii))

A Notice of Appeal was filed November 1, 2007, and an Appeal Brief was submitted April 1, 2008 in this application. Subsequently, a non-final Office Action issued June 25, 2008, rendering that first appeal moot.

Appellants are not aware of any other prior or pending appeal, judicial proceeding, or interference that may be related to, directly affect, or be directly affected by or have bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS (37 C.F.R. §41.37(c)(1)(iii))

A total of 28 claims have been introduced in this patent application. Claims 1-8, 11, 12, 17-20, 23 and 24 have been cancelled. Claims 9, 10, 13-16, 21, 22 and 25-28 remain pending. Every pending claim is rejected. This appeal requests reversal of all rejections.

IV. STATUS OF AMENDMENTS (37 C.F.R. §41.37(c)(1)(iv))

Appellants filed two amendments after the February 9, 2009, Final Office Action. An amendment, titled "Response to Final Office Action," was filed May 7, 2009, and amended claim 9. Although no Advisory Action has been received by Appellants and no respective Advisory Action is found on PAIR, it is Appellants' belief that the amendment has been entered as it eliminates one basis for rejection by returning claim 9 to its exact wording prior to the rejection, therby placing the claims in better form for appeal. A "Supplemental Response to Final Office Action" was filed November 5, 2009, in order to correct claim dependencies. As the Supplemental Response placed the claims in better condition for appeal, it is believed these amendments will have been entered as well. The claims now presented in Appendix A include all amendments submitted in response to the Final Office Action.

V. SUMMARY OF CLAIMED SUBJECT MATTER (37 C.F.R. §41.37(c)(1)(v))

The embodiments in pending claims 9, 10, 13-16, 21, 22 and 25-28 stem from the named inventors' discovery that submucosal administration of live attenuated vaccines reduces local adverse reactions that had previously been observed when such vaccines were administered via conventional routes for systemic application, particularly by intramuscular and intradermal administration. This reduction in local reactions is advantageous because it, for example, generally allows for less-attenuated vaccines to be used. Moreover, injection site abscesses are reduced or eliminated, eliminating the consequent disfigurement and meat value reduction. This discovery is not limited to any specific live attenuated vaccine. To the contrary, it is generally applicable to *all* live attenuated bacterial vaccines, independent of the bacterial strain or method of attenuation.

.

There are two independent claims, claims 9, and 21. They are summarized as follows:

A. **Claim 9** is directed to a method for reducing the amount of adverse reactions in a mammal at an injection site of a live attenuated bacterial vaccine, wherein the live vaccine comprises bacteria that would cause abscess formation if administered intramuscularly. The method comprises administering the vaccine submucosally, whereby the amount of adverse reactions at the injection site is reduced. The reduction is measured by the amount or size of abscesses at the mucosal injection site compared to an intramuscular injection site.

Claim 9 is generally supported by Appellants' specification at, for example, page 1, lines 20-28; and page 2, lines 4-28. *See also*, Appellants' specification, page 2, line 30 to page 3, line 23 (defining submucosal administration, and discussing administration sites, depths, and techniques for submucosal administration); page 3, line 25 to page 5, line 29 (discussing example bacteria that are generally suitable for use with the invention); page 6, lines 1-8 (discussing dosage ranges); page 6, lines 9-17 (discussing carrier materials); page 6, lines 18-26 (discussing adjuvants); and Examples 1-3 on page 7-9 (illustrating and corroborating Appellants' invention with four live bacterial strains and two animal species).

B. **Claim 21** is directed to a method for systemic application of live attenuated bacteria to a mammal. Live attenuated bacteria are administered that would cause abscess and/or lesion formation if administered intramuscularly or intradermally to the mammal. The method comprises administering the live attenuated bacteria submucosally, wherein any abscess and/or lesion formation at the site of the submucosal administration is less in total size than the abscess and/or lesion formation that would occur if the bacteria were instead administered intramuscularly or intradermally.

Claim 21 is supported by Appellants' specification at, for example, page 1, lines 20-28; page 2, lines 4-28; and Example 1, page 7, line 1 to page 8, line 20. *See also*, Appellants' specification, page 2, line 30 to page 3, line 23 (defining submucosal administration, and discussing administration sites, depths, and techniques for submucosal administration); page 3, line 25 to page 5, line 29 (discussing example bacteria that are generally suitable for use with the invention); page 6, lines 1-8 (discussing dosage ranges); page 6, lines 9-17 (discussing carrier materials); page 6, lines 18-26 (discussing adjuvants); and Examples 2-3 on page 8, line 21 to page 9, line 26 (further illustrating and corroborating Appellants' invention).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL (37 C.F.R. §41.37(c)(1)(vi))

Claims 9-11, 13-16 and 20-28 have been rejected under 35 U.S.C. §112 (first paragraph) for lacking enablement commensurate to the breadth of the claims. Appellants appeal this rejection.

Claims 9-11, 13-16 and 20 have been rejected under the written description requirement of 35 U.S.C. §112 (first paragraph) for failing to show possession of the entire scope of the claimed invention. The basis for this rejection has been rendered moot by the amendment to claim 9 in the Response submitted May 7, 2009, removing the previously proposed amendment on which the Examiner based this rejection.

VII. ARGUMENT (37 C.F.R. §41.37(c)(1)(vii))

Rejection of Claims 9-11, 13-16 and 20-28 under 35 U.S.C. 112, first paragraph, for lack of Enablement

"Claims 9-11, 13-16 and 20-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for protecting a mammal against *Streptococcus equi* infection by submucosal injection of a live attenuated *Streptococcus equi* strain (TW980), does not reasonably provide enablement for a method for protecting a mammal against all bacterial infection by sub mucosal injection of any live bacterial vaccines as claimed." (Final Office Action of February 9, 2009, page 2).

The Examiner has rejected all pending claims on the basis that the specification is not enabling for a method for protecting, which is not, in fact, the method Appellants are claiming. Reversal of this rejection is requested.

Appellants' claimed invention is a method for reducing adverse reactions (independent claim 9) and a method for systemic application of live attenuated bacteria wherein any abscess or lesion formation is less in total size than when administered intramuscularly or intradermally (independent claim 21). As it is a method for ameliorating the adverse consequences of vaccination, reducing the amount or size of lesions and abscesses, it is a method that would be used by those of skill in the art with known vaccines, vaccines that are known to be effective but cause injection site lesions or abscesses when administered conventionally. This is described in the Examples. The presently claimed invention is not directed to preparing vaccines. Appellants do not claim "...a method for protecting a mammal against all bacterial infection..." as asserted in this rejection.

The inventors discovered that submucosal administration of live attenuated vaccines reduces local adverse reactions that had previously been observed when such vaccines were administered via conventional routes for systemic application. This reduction in local reactions is advantageous because it, for example, generally allows for less-attenuated vaccines to be used, as well as reducing injury and, in food animals, meat spoilage. *See e.g.*,

Appellants' specification, page 1, lines 20-24. The inventors' discovery is not limited to any specific live attenuated bacterial vaccine.

i. *Claim 9*

Claim 9 is directed to a method for reducing the amount of adverse reactions in a mammal at an injection site of a live attenuated bacterial vaccine that comprises bacteria that cause abscess formation when administered intramuscularly. The method comprises administering the vaccine submucosally and the reduction is measured by the amount or size of the abscesses at the injection site.

This method stems from Appellants' discovery that submucosal administration of live attenuated vaccines reduces local adverse reactions that had previously been observed when the same vaccines were administered via conventional routes. Appellants' discovery is not limited to any specific live attenuated vaccine. To the contrary, Appellants' discovery is generally applicable to *all* live attenuated vaccines, independent of the bacterial strain or method of attenuation. This is corroborated by Examples 1-3 in Appellants' specification, which illustrate the reduction of local reactions by using submucosal administration instead of intramuscular administration with four different live bacterial strains and two different animal species.

ii. *Claims 10 and 13-16*

Claims 10 and 13-16 depend directly from claim 9. Claim 10 recites the invention wherein the vaccine is administered submucosally through the labiae. Claims 13-16 recite the invention wherein the mammal is a horse, a ruminant, a pig or a dog. Like claim 9, these claims have been rejected for not having sufficient description in the specification to enable the scope of live attenuated bacterial vaccines recited in the claims. Appellants respectfully submit that these claims are enabled for at least the same reasons as claim 9.

iii. *Claim 21*

Claim 21 is directed to a method for systemic application of live attenuated bacteria to a mammal. The bacteria cause abscess and/or lesion formation in the mammal if they are administered intramuscularly or intradermally to the mammal. The method comprises administering the bacteria submucosally to the mammal. Any abscess and/or lesion formation at the site of the submucosal administration is less in total size than the abscess and/or lesion formation that would occur if the bacteria are instead administered intramuscularly or intradermally to the mammal.

Appellants respectfully submit that claim 21 is enabled for at least the same reasons as claim 9.

vi. *Claims 22 and 25-28*

Claims 22 and 25-28 depend from claim 21. Claim 22 recites the method reduction of lesion or abscess size is compared to intramuscular administration. Claims 25-28 recite the invention wherein the mammal is a horse, a ruminant, a pig or a dog. Appellants respectfully submit that these claims are enabled for at least the same reasons as claim 21.

Appellants teach, and claim, changing the injection site from intramuscular or intradermal to submucosal using conventional vaccines, administering the same quantity but at a different injection site. Example 1 illustrates the invention using a conventional, commercial vaccine, fully enabling the claimed invention.

The enablement rejection suggests that the specification is insufficient to enable the scope of claims 9 and 21, and the claims dependent on them, because the specification fails to describe a method for protecting a mammal against all bacterial infection. The method alleged to not be enabled is not what is claimed. Appellants respectfully request reversal of this finding.

A claim satisfies the enablement requirement if the specification enables a skilled artisan to make and use the claimed invention without "undue experimentation." Even the necessity for "complex" experimentation does not necessarily equate to "undue" experimentation if those in the art typically engage in such experimentation. *In re Wands*,

858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). *See also,* MPEP §2164.01. Claims are enabled even if "a considerable amount" of experimentation is necessary where the experimentation is "merely routine" or the specification "provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. Whether a specification requires undue experimentation depends on multiple factors:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

See also, MPEP §2164.01(a).

Appellants submit that their claims satisfy the enablement requirement for reasons analogous to those in *Wands*. In *Wands*, the claims were directed to monoclonal IgM antibodies and an immunoassay using the antibodies. The court found that the claims were enabled even though a skilled artisan practicing the claimed invention would have to (1) obtain lymphocytes from an immunized animal; (2) fuse the lymphocytes with myeloma cells; and then (3) perform multiple screening steps to identify and separate out hybridomas, (3a) hybridomas producing antibodies to the desired antigen, and finally(3b) hybridomas producing antibodies having the claimed affinity. *Wands*, 858 F.2d at 739-740, 8 USPQ2d at 1404-1406. In finding enablement, the court noted: (1) the specification provided guidance for practicing the invention, (2) the specification provided working examples, (3) the level of skill in the art was high, (4) the methods needed to practice the invention were well known in the art, and (5) the nature of the technology involved screening to identify antibodies with the desired characteristics. *Wands*, 858 F.2d at 740, 8 USPQ2d at 1406. **Using reasoning analogous to *Wands*, Appellants' claims should also be found to satisfy the enablement requirement.**

Specifically:

1. **Appellants' specification provides guidance for practicing the invention.** For example, Appellants' specification provides generally suitable sites for

submucosal administration, administration depths and techniques, dosage ranges, suitable carrier materials, and suitable adjuvants. Appellants' specification also identifies a wide range of examples of live bacteria that are used in vaccines, which are generally suitable for use with the invention.

2. **Appellants' specification provides three working examples illustrating submucosal administration with four different live vaccines and two different host species.** These examples describe immunization according to the invention compared with intramuscular administration..

3. **The skill level in the art and nature of the technology are analogous to those in *Wands*.** In both cases PhD level biologists would be ordinary skilled practitioners.

4. **The methods needed to practice the invention are well known in the art.** As to live attenuated vaccines in particular, there was an extensive understanding in the art relating to methods for making and generally using live vaccines at the time Appellants' application was filed. The scientific literature from the time of Appellants' filing is replete with discussions relating to the development and use of live attenuated vaccines. Appellants illustrated their invention using a commercial vaccine in Example 1.

Appellants further submit that the level of experimentation required to administer a known vaccine subcutaneously by the procedures described in Appellants' specification by the ordinary skilled practitioner instead of administering it intramuscularly is minimal, far below the experimentation described as permissible in *Wands*. In fact, there is no experimentation involved beyond observing whether comparative injection site lesion or abscess formation is reduced by submucosal administration.

Simply put, Appellants' specification --- particularly when viewed in the context of the knowledge in the art at the time of Appellants' filing --- enables claim 9 and claim 21, and the claims dependent thereon. Accordingly, Appellants respectfully submit that the enablement rejection must be reversed.

D. ***Written Description Requirement under 35 U.S.C. §112 (first paragraph)***

Claims 9-11, 13-16 and 20 have been rejected under 35 U.S.C. §112 (first paragraph) for lack of written description in the specification. Specifically, the Examiner suggested that there is no support in the specification for reciting that the bacteria administered "replicate at the injection site," despite Appellants having pointed out that these words were found in line 12 on page 2. In order to advance the prosecution of this application, Appellants withdrew the proposed amendment introducing the apparently objectionable words in the Response to Final Office Action filed May 7, 2009, rendering this rejection moot.

VIII. DESCRIPTION OF CLAIMS APPENDIX (37 C.F.R. §41.37(c)(1)(viii))

An appendix containing a copy of all the claims involved in the appeal is attached.

IX. DESCRIPTION OF EVIDENCE APPENDIX (37 C.F.R. §41.37(c)(1)(ix))

None.

X. DESCRIPTION OF RELATED PROCEEDINGS APPENDIX (37 C.F.R. §41.37(c)(1)(x))

None.

XI. Fee payment and extension of time

Appellants authorize the Commissioner to charge Deposit Account No. 19-0365 for the fee under 37 CFR §41.20(b)(2) for filing this appeal.

Appellants have requested a two month extension of time in a Supplemental Response filed on November 5, 2009, which will extend the date for filing this Appeal Brief to November 8, 2009. Should a further extension to file this brief become necessary, Appellants authorize the Commissioner to charge Deposit Account No. 19-0365 for any required corresponding extension fee under 37 CFR §1.17(a)(5). Appellants do not believe that any other fee is due in connection with this filing. If, however, Appellants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No.19-0365. In addition, if there is ever any other fee deficiency or overpayment in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. 19-0365.

* * * * * * * * *

Appellants submit that the pending claims are in condition for allowance, and request that the rejections in the February 9, 2009 Final Office action be reversed, and this application be allowed.

Respectfully submitted,

/William M. BLACKSTONE/ Registration No. 29,772
William M. Blackstone, Registration No. 29,772
Intervet/Schering-Plough Animal Health
Patent Dept. K-6-1, 1990
Kenilworth, NJ 07033
(tel) 240 355 7129

APPENDIX A
Claims Appendix (37 C.F.R. §41.37(c)(1)(viii))

9. A method for reducing the amount of adverse reactions in a mammal at an injection site of a live attenuated bacterial vaccine, wherein:

the method comprises administering submucosally the vaccine, whereby the amount of adverse reactions at the injection site is reduced,

the live bacterial vaccine comprises bacteria that cause abscess formation when administered intramuscularly, and

the reduction of the amount of adverse reactions is measured by the amount or size of abscesses or lesions at the mucosal injection site compared to an intramuscular injection site.

10. The method according to claim 9, wherein the vaccine is administered into the submucosa of the labiae.

13. The method according to claim 9, wherein the mammal is a horse.

14. The method according to claim 9, wherein the mammal is a ruminant.

15. The method according to claim 9, wherein the mammal is a pig.

16. The method according to claim 9, wherein the mammal is a dog.

21. A method for systemic application of live attenuated bacteria to a mammal, wherein:

the method comprises administering the live attenuated bacteria submucosally to the mammal,

the live attenuated bacteria cause abscess and/or lesion formation in the mammal if the live attenuated bacteria are instead administered intramuscularly or intradermally to the mammal, and

any abscess and/or lesion formation at the site of the submucosal administration is less in total size than the abscess and/or lesion formation that would occur if the bacteria are instead administered intramuscularly or intradermally to the mammal.

22. A method according to claim 21, wherein the live attenuated bacteria cause abscess and/or lesion formation in the mammal if the live attenuated bacteria are administered intramuscularly to the mammal.

25. The method according to claim 21, wherein the mammal is a horse.

26. The method according to claim 21, wherein the mammal is a ruminant.

27. The method according to claim 21, wherein the mammal is a pig.

28. The method according to claim 21, wherein the mammal is a dog.

APPENDIX B
Evidence Appendix (37 C.F.R. §41.37(c)(1)(ix))

None.

APPENDIX C
Related Proceedings Appendix (37 C.F.R. §41.37(c)(1)(x))

None.